

**In the Specification:**

Pages 1 to 5, please delete these pages in their entirety and substitute therefor the following:

**CROSS-REFERENCE**

This is a divisional of copending U.S. Patent Application, Ser. No. 09/744,892, filed January 31, 2001.

**Background of the Invention****1. Field of the Invention**

The present invention relates to a method of promoting hair growth and/or decreasing hair fall-out using certain cyclic compounds.

**2. Description of the Related Art**

The human scalp normally harbors 100,000 to 150,000 hair follicles or hairs. The hair follicles or hair roots or hair bulbi are the hair-forming organs. The long, strong hairs, which build up the hair coverage of the head, are referred to as terminal hairs. The very fine, very short hairs, barely protruding over the surface of the skin, at the edges of the hair coverage on the head, are referred to as fuzz hair, or as vellus hair. The growth of hair is not continuous, but cyclical. Three growth phases are identified: (1) the anagen, during which the hair grows, (2) the katagen, during which the hair follicle prepares for the next phase, the telogen, and the previously growing hair is converted into a resting hair or club hair and (3) the telogen, that is, the resting phase during which hair growth ceases completely. In response to a signal, which is not identified at the present time, the telogen follicle awakens to a new activity or commences a new anagen,

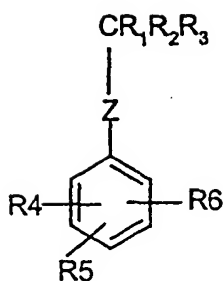
in the course of which a new hair grows and the existing club hair is shed. This hair growth cycle proceeds unchanged during the whole life and, moreover equally in the case of the long, strong terminal hair as well as in the case of the very short fuzz hair or vellus hair. A prerequisite for a normal growth of a healthy head of hair is a perfectly functioning organism and an optimum supply for it of all the necessary nutrients and auxiliary materials. Many factors can affect the growth of the hair on the head, namely wrong nutrition, deficient nutrition, severe illnesses, medicinal drugs, emotional stresses and temporary disorders of the hormone balance in the organism. A loss of hair, brought about by such factors, usually is temporary.

### **Summary of the Invention**

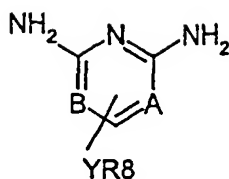
It is therefore an object of the present invention to provide method of promoting hair growth and/or reducing hair loss by applying certain cyclic compounds.

According to the invention this method comprises the steps of:

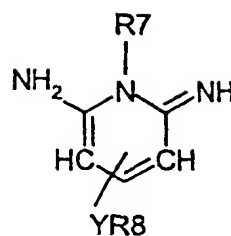
- a) providing an agent comprising at least one of a compound of formula (I), a compound of formula (II) and a compound of formula (III) and a physiologically compatible salt thereof:



(I)



(II)



(III)

wherein **A** and **B**, independently of each other, are each a CH group or a nitrogen atom, with the proviso that at least one of **A** and **B** is the CH group;

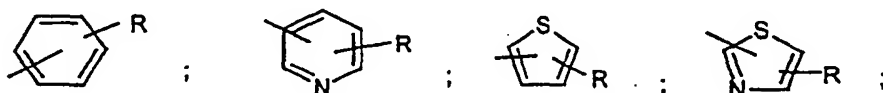
**Y** represents -O-,  $-(CH_2)_n$ -, -NH-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-, -N=N-, -CH=CH-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-, -N=CH-, -CH=N-,  $-(CH_2-CH_2-O)_m$ - or  $-(O-CH_2-CH_2)_m$ -, with m and n, independently of each other, equal to 1, 2, 3 or 4;

**Z** represents -NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH=CH- or -CH<sub>2</sub>-NH-;

**R1** represents -H, -OH or a hydroxyalkyl group having one to four carbon atoms;

**R2** represents -H, a cyclopropyl group or an alkyl group containing from one to four carbon atoms;

**R3** represents a hydroxyalkyl group having one to two carbon atoms, -CH<sub>2</sub>-X or -CHX<sub>2</sub>, -COCH<sub>3</sub>, -CF<sub>3</sub>, -CH<sub>3</sub> or



wherein X represents F, Cl, Br or I and R represents -NO<sub>2</sub>, -SO<sub>2</sub>CH<sub>3</sub>, -CF<sub>3</sub>, -CHF<sub>2</sub>, -CH<sub>2</sub>F, -F or -Cl;

**R4, R5 and R6**, independently of each other, each represent -NO<sub>2</sub>, -CF<sub>3</sub>, -CHF<sub>2</sub>, -CH<sub>2</sub>F, -F, -Cl, -Br or -H;

**R7** represents -OH, -OSO<sub>3</sub>H, -OALK or -OCOCH<sub>3</sub>, wherein ALK represents an alkyl group having one to four carbon atoms;

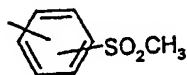
**R8** represents an alkyl group with one to six carbon atoms, a hydroxyalkyl group having from one to six carbon atoms, a hydroxyalkenyl group having from two to six carbon atoms, an aryl group, a heteroaryl group or an alkenyl carboxylic acid group having two to six carbon atoms;

with the proviso that, when **R4** is at a 2 position and represents -NO<sub>2</sub> in the compound of formula (I), **R5** is in a 4 position and represents -CF<sub>3</sub>, **R6** represents -H and **ZCR1R2R3** represents -NH-CH=CH-CHOH-CH<sub>2</sub>OH;

b) applying the agent to hair and scalp in an amount sufficient for promoting of hair growth and/or decreasing hair loss; and

c) leaving the agent on the hair and scalp for a predetermined time interval.

Preferred compounds of formula (I) for use as the agent in the method of the invention are those in which **Z** is -NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH=CH- or -CH<sub>2</sub>-NH-, **R1** is -OH, -CH<sub>2</sub>OH or -CH<sub>2</sub>CH<sub>2</sub>OH, **R2** is -H, -CH<sub>3</sub> or -C<sub>2</sub>H<sub>5</sub>; and **R3** represents



a hydroxyalkyl group containing from one to two carbon atoms, -CH<sub>2</sub>F, -CH<sub>2</sub>Cl,

-CH<sub>2</sub>Br, -CH<sub>2</sub>I, -CF<sub>3</sub> or -CH<sub>3</sub>, and **R4**, **R5** and **R6** are each, independently of each other, -NO<sub>2</sub>, -CF<sub>3</sub>, -CHF<sub>2</sub>, -CH<sub>2</sub>F, -F, -Cl, -Br or -H. However the compounds of formula (I) are particularly preferred, in which **R1** is -OH or -CH<sub>2</sub>OH, **R2** is -H or -CH<sub>3</sub>, **R3** is a hydroxyalkyl group with one to two carbon atoms, -CH<sub>2</sub>F, -CH<sub>2</sub>Cl, -CH<sub>2</sub>Br, -CH<sub>2</sub>I, -CF<sub>3</sub> or -CH<sub>3</sub>, and **R4** represents -NO<sub>2</sub>, **R5** represents -CF<sub>3</sub> and **R6** represents -H. The compounds of formula (I) are especially particularly preferred in which Z represents -NH-CH<sub>2</sub>-, **R1** represents -OH, **R2** represents -H, **R3** represents -CH<sub>2</sub>OH, **R4** represents -NO<sub>2</sub>, **R5** represents -CF<sub>3</sub> and **R6** represents -H.

Preferred compounds of formula (II) for use as the agent in the method of the invention are those in which the **A** represents the CH group, **B** represents the CH group or a nitrogen atom, **Y** represents -N=N-, -(CH<sub>2</sub>)<sub>n</sub>-, -CH=CH-, -N=CH- or -CH=N-, and **R8** represents an alkyl group with one to six carbon atoms, a hydroxyalkyl group having from one to six carbon atoms, a phenyl group, a benzyl group or a pyridyl group. However compounds of formula (II) are especially preferred, in which A and B both represent a -CH- group, Y represents -N=N- and **R8** represents a pyridyl group.

Preferred compounds of formula (III) for use as the agent in the method of the invention are those in which **Y** represents -N=N-, -(CH<sub>2</sub>)<sub>n</sub>-, -CH=CH-, -N=CH- or -CH=N-; **R7** represents -OH, -OSO<sub>3</sub>H or -OALK, wherein ALK is the alkyl group having one to four carbon atoms and **R8** represents an alkyl group with one to six carbon atoms, a hydroxyalkyl group having from one to six carbon atoms, a phenyl group, a benzyl group or a pyridyl group. Compounds of formula

(III) which are especially preferred are those in which Y represents -N=N-, **R7** represents -OH (including the corresponding tautomeric N-oxides) and **R8** represents a pyridyl group.

The following exemplary compounds are preferred for use as the agent in the method of the invention: 1-[N-(2'-nitro-4'-trifluoro-methylphenyl)amino]-3-chloro-2-hydroxypropanol, 1-[N-(2'-nitro-4'-trifluoro-methylphenyl)amino]-2-hydroxy-2-trifluoromethylethane, 1-[N-(2'-nitro-4'-trifluoro-methylphenyl)-amino]-propan-2,3-diol, 1-(2'-nitro-4'-trifluoro-methylphenyl)-1-butene-3,4-diol, 2,6-diamino-3-((pyridin-3-yl)-azo)pyridine and 2,6-diamino-3-((pyridin-3-yl)-azo)pyridin-1-oxide. Of these exemplary compounds 1-[N-(2'-nitro-4'-trifluoro-methyl-phenyl)amino]-2,3-propylene glycol and 2,6-diamino-3-((pyridin-3-yl)azo)pyridine and combinations thereof are particularly preferred.

The cosmetic agent according to the invention may be in any form suitable for application to hair and scalp, especially in the form of an aqueous, alcoholic or aqueous-alcoholic preparation, such as a solution, gel, cream, emulsion or dispersion. It is also possible to dispense this agent as a spray or a foam from a pressurized container with conventional blowing agents, which are liquefied under pressure, for example, chlorofluoroalkanes, such as CCl<sub>3</sub>F, CCl<sub>2</sub>F<sub>2</sub>, C<sub>2</sub>Cl<sub>3</sub>F<sub>3</sub>, CCl<sub>2</sub>F<sub>2</sub>, CHCl<sub>2</sub>F<sub>2</sub> and (CClF<sub>2</sub>)<sub>2</sub>, highly volatile hydrocarbons, such as n-butane, and n-propane, or also dimethyl ether, carbon dioxide, nitrous oxide, nitrogen, methylene chloride and 1,1,1-trichloromethane.

The forms, in which the inventive cosmetic agents are prepared, may also remain on the hair and the scalp and comprise, for example, insertion materials,

combing gels, hair pomades, hair oils and hair treatments. Especially preferred are the hair treatments as well as so-called "sustained release" preparations, which emit the active ingredient uniformly over a longer period of time, or the producing of the compounds of formulae (I) and (II) as liposomes. --.

Page 6, lines 1 to 7, please delete these lines in their entirety.